WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Wednesday, March 29, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ	
☐	L33	l28 and l24	22
☐	L32	L31 and l24	0
☐	L31	L29 not @ay>2002	171
☐	L30	L29 not ay>2002	0
☐	L29	L28 and l25	202
☐	L28	DMPS	4375
☐	L27	L26 and adjuvant	11
☐	L26	L25 and l24	25
☐	L25	213Bi or (bismuth 213) or (213 bismuth)	584
☐	L24	(424/1.49,1.53,1.57,179.1,181.1)![CCLS]	1160
☐	L23	L22 and L6	9
☐	L22	(Scheinberg or mcdevitt or jaggi).in.	666
☐	L21	(20020058007 or 20030023050).pn.	2
☐	L20	L18 and L9	4
☐	L19	L18 and L17	0
☐	L18	furosemide or chlorthiazide or hydrochlorothiazide or bumex	4580
☐	L17	L16 and L15	5
☐	L16	diethylenetriamine$	25649
☐	L15	L13 not @py>2003	7
☐	L14	L13 not py>2003	0
☐	L13	L12 and L11	17
☐	L12	huM195	55
☐	L11	L10 and L9	24
☐	L10	cd33	1651
☐	L9	L7 and L8	177
☐	L8	conjugat$ or coupl$ or attach$ or link$	3399816
☐	L7	L6 and antibod$	182
☐	L6	actinium	932
☐	L5	L3 and nephrotoxic$	19
☐	L4	L3 and nephrotocix$	0
☐	L3	radioimmunotherap$	1200

☐	L2	radioimmunotherapy	1137
☐	L1	radioimmunothearpy	0

END OF SEARCH HISTORY

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 9	JAN 30	Saved answer limit increased
NEWS 10	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 12	FEB 22	Status of current WO (PCT) information on STN
NEWS 13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 17	FEB 28	TOXCENTER reloaded with enhancements
NEWS 18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 19	MAR 01	INSPEC reloaded and enhanced
NEWS 20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 21	MAR 08	X.25 communication option no longer available after June 2006
NEWS 22	MAR 22	EMBASE is now updated on a daily basis

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:18:17 ON 29 MAR 2006

=> file medline
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:18:26 ON 29 MAR 2006

 FILE LAST UPDATED: 28 MAR 2006 (20060328/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s bismuth
L1         5212 BISMUTH

=> s actinium
L2           93 ACTINIUM

=> s DMPS or DMSA
            356 DMPS
           1428 DMSA
              1 DMSAS
           1429 DMSA
                  (DMSA OR DMSAS)
L3         1693 DMPS OR DMSA

=> s l3 and l2
L4            1 L3 AND L2

=> s l3 adn l1
MISSING OPERATOR L3 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l3 and l1
L5            7 L3 AND L1

=> kidney or renal or nephro?
KIDNEY IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

```
=> s kidney or renal or nephro?
        487300 KIDNEY
         55703 KIDNEYS
        500183 KIDNEY
                 (KIDNEY OR KIDNEYS)
        356537 RENAL
            23 RENALS
        356545 RENAL
                 (RENAL OR RENALS)
         94617 NEPHRO?
L6      638909 KIDNEY OR RENAL OR NEPHRO?

=> s l6 adn l5
MISSING OPERATOR L6 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l6 and l5
L7            5 L6 AND L5

=> d ibib 1-5

L7   ANSWER 1 OF 5     MEDLINE on STN
ACCESSION NUMBER:   2005285089     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15930310
TITLE:              Efforts to control the errant products of a targeted in
                    vivo generator.
AUTHOR:             Jaggi Jaspreet Singh; Kappel Barry J; McDevitt Michael R;
                    Sgouros George; Flombaum Carlos D; Cabassa Catalina;
                    Scheinberg David A
CORPORATE SOURCE:   Molecular Pharmacology and Chemistry Program, Memorial
                    Sloan-Kettering Cancer Center, New York, New York 10021,
                    USA.
CONTRACT NUMBER:    P01-33049 (NCI)
                    R01-CA 55349
SOURCE:             Cancer research, (2005 Jun 1) Vol. 65, No. 11, pp. 4888-95.
                    Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200507
ENTRY DATE:         Entered STN: 20050603
                    Last Updated on STN: 20050729
                    Entered Medline: 20050728

L7   ANSWER 2 OF 5     MEDLINE on STN
ACCESSION NUMBER:   2002145123     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11877598
TITLE:              Fanconi's syndrome, acute renal failure, and
                    tonsil ulcerations after colloidal bismuth
                    subcitrate intoxication.
AUTHOR:             Hruz Petr; Mayr Michael; Low Roland; Drewe Jurgen; Huber
                    Gerold
CORPORATE SOURCE:   Department of Internal Medicine Clinic B, Division of
                    Transplantation Immunology and Nephrology, University
                    Hospital Basel, Basel, Switzerland.. petrhruz@hotmail.com
SOURCE:             American journal of kidney diseases : the official journal
                    of the National Kidney Foundation, (2002 Mar) Vol. 39, No.
                    3, pp. E18.
                    Journal code: 8110075. E-ISSN: 1523-6838.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      (CASE REPORTS)
```

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020320
Entered Medline: 20020319

L7 ANSWER 3 OF 5 MEDLINE on STN
ACCESSION NUMBER: 97021921 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8868281
TITLE: Evaluation of dithiol chelating agents as potential adjuvants for anti-IL-2 receptor lead or **bismuth** alpha radioimmunotherapy.
AUTHOR: Jones S B; Tiffany L J; Garmestani K; Gansow O A; Kozak R W
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, National Naval Medical Center, Bethesda, MD 20889, USA.
SOURCE: Nuclear medicine and biology, (1996 Feb) Vol. 23, No. 2, pp. 105-13.
Journal code: 9304420. ISSN: 0969-8051.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970130

L7 ANSWER 4 OF 5 MEDLINE on STN
ACCESSION NUMBER: 92260104 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1583409
TITLE: Development of a therapeutic procedure for **bismuth** intoxication with chelating agents.
AUTHOR: Slikkerveer A; Jong H B; Helmich R B; de Wolff F A
CORPORATE SOURCE: Toxicology Laboratory, University Hospital Leiden, The Netherlands.
SOURCE: The Journal of laboratory and clinical medicine, (1992 May) Vol. 119, No. 5, pp. 529-37.
Journal code: 0375375. ISSN: 0022-2143.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920626
Last Updated on STN: 19970203
Entered Medline: 19920618

L7 ANSWER 5 OF 5 MEDLINE on STN
ACCESSION NUMBER: 90215354 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2323603
TITLE: **Bismuth** induced encephalopathy caused by tri potassium dicitrato bismuthate in a patient with chronic **renal** failure.
AUTHOR: Playford R J; Matthews C H; Campbell M J; Delves H T; Hla K K; Hodgson H J; Calam J
CORPORATE SOURCE: Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London.
SOURCE: Gut, (1990 Mar) Vol. 31, No. 3, pp. 359-60.
Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900622
Last Updated on STN: 19970203
Entered Medline: 19900515

=> d ibib abs 4

L7 ANSWER 4 OF 5 MEDLINE on STN
ACCESSION NUMBER: 92260104 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1583409
TITLE: Development of a therapeutic procedure for **bismuth** intoxication with chelating agents.
AUTHOR: Slikkerveer A; Jong H B; Helmich R B; de Wolff F A
CORPORATE SOURCE: Toxicology Laboratory, University Hospital Leiden, The Netherlands.
SOURCE: The Journal of laboratory and clinical medicine, (1992 May) Vol. 119, No. 5, pp. 529-37.
Journal code: 0375375. ISSN: 0022-2143.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920626
Last Updated on STN: 19970203
Entered Medline: 19920618

AB Although **bismuth** poisoning is still a rare phenomenon, the increasing use of **bismuth**-containing drugs warrants a systematic approach to the treatment of **bismuth** overdose. An effective method of enhancing the elimination of toxic amounts of **bismuth** from the body has not been reported. Therefore we performed a study to select the best chelator to treat **bismuth** poisoning. Dimercaprol (BAL), meso-2,3-dimercaptosuccinic acid (**DMSA**), D,L-2,3-dimercapto-propane-I-sulfonic acid (**DMPS**), D-penicillamine (D-PEN), N-acetyl-D,L-penicillamine (Ac-PEN), thiopronine (TP), sodium-calcium edetate (EDTA) and deferoxamine (DFO) were tested with an in vitro model of equilibrium dialysis and an in vivo model of rats poisoned with **bismuth**. The rats (n = 6 per substance tested) were treated with the chelators in intraperitoneal doses of 250 mumol/kg.day for 3 consecutive days. Afterward, tissue and blood samples were collected. **Bismuth** concentrations were determined with electrothermal atomic absorption spectrometry in serum, buffer, urine, blood, brain, **kidney**, liver, spleen, and bone. Using in vitro results, we constructed a ranking of chelating agents; it appeared not to predict the in vivo results. The dithiol compounds (**DMPS**, **DMSA** and BAL) were effective in most organs (especially in **kidney** and liver) resulting in a higher elimination of **bismuth** in urine by **DMPS** and BAL. BAL was the only chelator effective in lowering brain **bismuth** concentrations, whereas treatment with EDTA resulted in increased brain **bismuth** levels. For D-PEN and DFO, no effects could be demonstrated. For clinical practice, **DMSA** and **DMPS** may well be the chelators of choice; the application of BAL should be reserved for very severe cases of poisoning because of its own toxicity.

=> d his

(FILE 'HOME' ENTERED AT 11:18:17 ON 29 MAR 2006)

```
     FILE 'MEDLINE' ENTERED AT 11:18:26 ON 29 MAR 2006
L1          5212 S BISMUTH
L2            93 S ACTINIUM
L3          1693 S DMPS OR DMSA
L4             1 S L3 AND L2
L5             7 S L3 AND L1
L6        638909 S KIDNEY OR RENAL OR NEPHRO?
L7             5 S L6 AND L5

=> s l2 adn l6
MISSING OPERATOR L2 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l2 and l6
L8            12 L2 AND L6

=> s accum? or reten?
        227213 ACCUM?
         80245 RETEN?
L9       303767 ACCUM? OR RETEN?

=> s l9 and l8
L10            4 L9 AND L8

=> s tox
L11          646 TOX

=> s tox?
L12       543991 TOX?

=> s l12 and l10
L13            1 L12 AND L10

=> d ibib

L13  ANSWER 1 OF 1     MEDLINE on STN
ACCESSION NUMBER:    2005576806     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 16253811
TITLE:               Biodistribution of 225Ra citrate in mice: retention
                     of daughter radioisotopes in bone.
AUTHOR:              Kennel Stephen J; Lankford Trish; Garland Marc; Sundberg
                     John P; Mirzadeh Saed
CORPORATE SOURCE:    Division of Life Sciences, Oak Ridge National Lab, Oak
                     Ridge, TN 37831, USA.. kennelsj@ornl.gov
SOURCE:              Nuclear medicine and biology, (2005 Nov) Vol. 32, No. 8,
                     pp. 859-67.
                     Journal code: 9304420. ISSN: 0969-8051.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200603
ENTRY DATE:          Entered STN: 20051029
                     Last Updated on STN: 20060310
                     Entered Medline: 20060309


=> d l10 ibib 1-4

L10  ANSWER 1 OF 4     MEDLINE on STN
ACCESSION NUMBER:    2005576806     MEDLINE
```

DOCUMENT NUMBER: PubMed ID: 16253811
TITLE: Biodistribution of 225Ra citrate in mice: **retention** of daughter radioisotopes in bone.
AUTHOR: Kennel Stephen J; Lankford Trish; Garland Marc; Sundberg John P; Mirzadeh Saed
CORPORATE SOURCE: Division of Life Sciences, Oak Ridge National Lab, Oak Ridge, TN 37831, USA.. kennelsj@ornl.gov
SOURCE: Nuclear medicine and biology, (2005 Nov) Vol. 32, No. 8, pp. 859-67.
Journal code: 9304420. ISSN: 0969-8051.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 20051029
Last Updated on STN: 20060310
Entered Medline: 20060309

L10 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2005285089 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15930310
TITLE: Efforts to control the errant products of a targeted in vivo generator.
AUTHOR: Jaggi Jaspreet Singh; Kappel Barry J; McDevitt Michael R; Sgouros George; Flombaum Carlos D; Cabassa Catalina; Scheinberg David A
CORPORATE SOURCE: Molecular Pharmacology and Chemistry Program, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.
CONTRACT NUMBER: P01-33049 (NCI)
R01-CA 55349
SOURCE: Cancer research, (2005 Jun 1) Vol. 65, No. 11, pp. 4888-95.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 20050603
Last Updated on STN: 20050729
Entered Medline: 20050728

L10 ANSWER 3 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2001045501 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10941530
TITLE: Evaluation of 225Ac for vascular targeted radioimmunotherapy of lung tumors.
AUTHOR: Kennel S J; Chappell L L; Dadachova K; Brechbiel M W; Lankford T K; Davis I A; Stabin M; Mirzadeh S
CORPORATE SOURCE: Life Sciences Division, Oak Ridge National Laboratory, Tennessee 37831-6101, USA.. kennelsj@ornl.gov
CONTRACT NUMBER: HL09718 (NHLBI)
SOURCE: Cancer biotherapy & radiopharmaceuticals, (2000 Jun) Vol. 15, No. 3, pp. 235-44.
Journal code: 9605408. ISSN: 1084-9785.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

Entered Medline: 20001206

L10 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 67184081 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6029424
TITLE: The effects of desferrioxamine on the **retention** of actinide elements in the rat.
AUTHOR: Taylor D M
SOURCE: Health physics, (1967 Feb) Vol. 13, No. 2, pp. 135-40. Journal code: 2985093R. ISSN: 0017-9078.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196709
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19990129
Entered Medline: 19670913

=> d ibib abs l10 4

L10 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 67184081 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6029424
TITLE: The effects of desferrioxamine on the **retention** of actinide elements in the rat.
AUTHOR: Taylor D M
SOURCE: Health physics, (1967 Feb) Vol. 13, No. 2, pp. 135-40. Journal code: 2985093R. ISSN: 0017-9078.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196709
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19990129
Entered Medline: 19670913

=> d his

(FILE 'HOME' ENTERED AT 11:18:17 ON 29 MAR 2006)

FILE 'MEDLINE' ENTERED AT 11:18:26 ON 29 MAR 2006
L1 5212 S BISMUTH
L2 93 S ACTINIUM
L3 1693 S DMPS OR DMSA
L4 1 S L3 AND L2
L5 7 S L3 AND L1
L6 638909 S KIDNEY OR RENAL OR NEPHRO?
L7 5 S L6 AND L5
L8 12 S L2 AND L6
L9 303767 S ACCUM? OR RETEN?
L10 4 S L9 AND L8
L11 646 S TOX
L12 543991 S TOX?
L13 1 S L12 AND L10

=> s francium
L14 12 FRANCIUM

=> s l14 and l6

L15 1 L14 AND L6

=> d ibib

L15 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 2005285089 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15930310
TITLE: Efforts to control the errant products of a targeted in vivo generator.
AUTHOR: Jaggi Jaspreet Singh; Kappel Barry J; McDevitt Michael R; Sgouros George; Flombaum Carlos D; Cabassa Catalina; Scheinberg David A
CORPORATE SOURCE: Molecular Pharmacology and Chemistry Program, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.
CONTRACT NUMBER: P01-33049 (NCI)
R01-CA 55349
SOURCE: Cancer research, (2005 Jun 1) Vol. 65, No. 11, pp. 4888-95.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 20050603
Last Updated on STN: 20050729
Entered Medline: 20050728

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.33	7.54

FILE 'CAPLUS' ENTERED AT 11:25:59 ON 29 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 29 Mar 2006 VOL 144 ISS 14
FILE LAST UPDATED: 27 Mar 2006 (20060327/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s bismuth
127908 BISMUTH
5 BISMUTHS
L16 127908 BISMUTH
(BISMUTH OR BISMUTHS)

```
=> s actinium
          2529 ACTINIUM
             4 ACTINIUMS
L17       2530 ACTINIUM
                (ACTINIUM OR ACTINIUMS)

=> s DMPS or DMSA
           510 DMPS
           743 DMSA
L18       1149 DMPS OR DMSA

=> s kidney or renal or nephro?
        276002 KIDNEY
         65528 KIDNEYS
        296836 KIDNEY
                (KIDNEY OR KIDNEYS)
        143848 RENAL
            11 RENALS
        143853 RENAL
                (RENAL OR RENALS)
         38908 NEPHRO?
L19     337893 KIDNEY OR RENAL OR NEPHRO?

=> s l19 and l17
L20         32 L19 AND L17

=> s l20 and l18
L21          1 L20 AND L18

=> s l20 and adjuvant
          32323 ADJUVANT
          17568 ADJUVANTS
          40470 ADJUVANT
                (ADJUVANT OR ADJUVANTS)
L22           4 L20 AND ADJUVANT

=> d ibib 1-4

L22  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:467296  CAPLUS
DOCUMENT NUMBER:          143:93157
TITLE:                    Efforts to Control the Errant Products of a Targeted
                          In vivo Generator
AUTHOR(S):                Jaggi, Jaspreet Singh; Kappel, Barry J.; McDevitt,
                          Michael R.; Sgouros, George; Flombaum, Carlos D.;
                          Cabassa, Catalina; Scheinberg, David A.
CORPORATE SOURCE:         Molecular Pharmacology and Chemistry Program,
                          Sloan-Kettering Cancer Center, New York, NY, 10021,
                          USA
SOURCE:                   Cancer Research (2005), 65(11), 4888-4895
                          CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:                American Association for Cancer Research
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          41    THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:802241  CAPLUS
DOCUMENT NUMBER:          141:273653
TITLE:                    Methods of protection from toxicity of alpha emitting
                          elements during radioimmunotherapy
```

INVENTOR(S): Scheinberg, David; McDevitt, Michael R.; Jaggi, Jaspreet
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004191169	A1	20040930	US 2004-806905		20040323
AU 2004273775	A1	20050331	AU 2004-273775		20040323
PRIORITY APPLN. INFO.:			US 2003-457503P	P	20030325
			WO 2004-US8817	W	20040323

L22 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:141669 CAPLUS
DOCUMENT NUMBER: 140:216171
TITLE: Anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic cancers
INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schulke, Norbert; Gardner, Jason; Ma, Dangshe
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 151 pp., Cont.-in-part of Appl. No. PCT/US02/33944.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004033229	A1	20040219	US 2003-395894		20030321
WO 2003034903	A2	20030501	WO 2002-US33944		20021023
WO 2003034903	A3	20031030			
WO 2003034903	B1	20040513			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004161776	A1	20040819	US 2003-695667		20031027
US 2005215472	A1	20050929	US 2004-976352		20041027
PRIORITY APPLN. INFO.:			US 2001-335215P	P	20011023
			US 2002-362747P	P	20020307
			US 2002-412618P	P	20020920
			WO 2002-US33944	A2	20021023
			US 2003-395894	A2	20030321
			US 2003-695667	A2	20031027

L22 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:334823 CAPLUS
DOCUMENT NUMBER: 138:352761
TITLE: Anti-prostate specific membrane antigen (PSMA)

	antibodies and fragments for cancer diagnosis and therapy and antitumor screening
INVENTOR(S):	Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schuelke, Norbert; Gardner, Jason; Ma, Dangshe
PATENT ASSIGNEE(S):	PSMA Development Company, L.L.C., USA
SOURCE:	PCT Int. Appl., 238 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464239	AA	20030501	CA 2002-2464239	20021023
EP 1448588	A2	20040825	EP 2002-802198	20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005523683	T2	20050811	JP 2003-537481	20021023
US 2004033229	A1	20040219	US 2003-395894	20030321
US 2004161776	A1	20040819	US 2003-695667	20031027
US 2005215472	A1	20050929	US 2004-976352	20041027

PRIORITY APPLN. INFO.:	US 2001-335215P	P	20011023
	US 2002-362747P	P	20020307
	US 2002-412618P	P	20020920
	WO 2002-US33944	W	20021023
	US 2003-395894	A2	20030321
	US 2003-695667	A2	20031027

=> d kwic 4

L22 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

IT Immunostimulants
(**adjuvants**; anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening)

IT Affinity
Angiogenesis inhibitors
Animal
Antitumor agents
Brain, neoplasm
Chromophores
Combinatorial library
Cytolysis
Cytotoxic agents
DNA sequences
Epitopes
Fluorescent substances
Gamma ray

Genetic vectors
Human
Hybridoma
Immunomodulators
Immunostimulants
Kidney, neoplasm
Labels
Luminescent substances
Lung, neoplasm
Mammalia
Mammary gland, neoplasm
Melanoma
Pancreas, neoplasm
Prognosis
Prostate gland, neoplasm
Protein sequences
Sarcoma
Stabilizing agents
Test kits
Testis, neoplasm
Vaccines
(anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening)

IT **Kidney**, neoplasm
(**renal** cell carcinoma; anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening)

IT Carcinoma
(**renal** cell; anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening)

IT 50-07-7, Mitomycin C 51-21-8, 5-Fluorouracil 57-22-7, Vincristine 59-05-2, Methotrexate 147-94-4, ARA-C 148-82-3, Melphalan 305-03-3, Chlorambucil 2998-57-4, Estramustine 10043-66-0, Iodine-131, biological studies 10098-91-6, Yttrium-90, biological studies 11056-06-7, Bleomycin 13233-32-4, Radium-224, biological studies 13967-65-2, Holmium-166, biological studies 13981-25-4, Copper-64, biological studies 14158-31-7, Iodine-125, biological studies 14265-75-9, Lutetium-177, biological studies 14265-85-1, **Actinium**-225, biological studies 14913-49-6, Bismuth-212, biological studies 15092-94-1, Lead-212, biological studies 15623-45-7, Radium-223, biological studies 15663-27-1, cis-Platinum 15715-08-9, Iodine-123, biological studies 15755-39-2, Astatine-211, biological studies 15757-86-5, Copper-67, biological studies 15765-39-6, Bromine-77, biological studies 15766-00-4, Samarium-153, biological studies 15776-20-2, Bismuth-213, biological studies 23214-92-8, Doxorubicin 33069-62-4, Paclitaxel 33419-42-0, Etoposide 53643-48-4, Vindesine 81284-87-9, Rhodium-86, biological studies 81284-89-1, Rhodium-88, biological studies 83869-56-1, GM-CSF 110417-88-4, Dolastatin 10 113440-58-7, Calicheamicin 114797-28-3, Esperamicin 114977-28-5, Docetaxel 160800-57-7, Auristatin E 161485-77-4, Auristatin PHE
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening)

=> d his

(FILE 'HOME' ENTERED AT 11:18:17 ON 29 MAR 2006)

FILE 'MEDLINE' ENTERED AT 11:18:26 ON 29 MAR 2006
L1 5212 S BISMUTH

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L2            93 S ACTINIUM
L3          1693 S DMPS OR DMSA
L4             1 S L3 AND L2
L5             7 S L3 AND L1
L6        638909 S KIDNEY OR RENAL OR NEPHRO?
L7             5 S L6 AND L5
L8            12 S L2 AND L6
L9        303767 S ACCUM? OR RETEN?
L10            4 S L9 AND L8
L11          646 S TOX
L12       543991 S TOX?
L13            1 S L12 AND L10
L14           12 S FRANCIUM
L15            1 S L14 AND L6

     FILE 'CAPLUS' ENTERED AT 11:25:59 ON 29 MAR 2006
L16       127908 S BISMUTH
L17         2530 S ACTINIUM
L18         1149 S DMPS OR DMSA
L19       337893 S KIDNEY OR RENAL OR NEPHRO?
L20           32 S L19 AND L17
L21            1 S L20 AND L18
L22            4 S L20 AND ADJUVANT

=> s diuretic or lasix or furosemide
          15447 DIURETIC
          12832 DIURETICS
          20335 DIURETIC
                (DIURETIC OR DIURETICS)
            175 LASIX
           7226 FUROSEMIDE
              1 FUROSEMIDES
           7226 FUROSEMIDE
                (FUROSEMIDE OR FUROSEMIDES)
L23       25120 DIURETIC OR LASIX OR FUROSEMIDE

=> s l23 and l20
L24            2 L23 AND L20

=> s l23 and l16
L25           44 L23 AND L16

=> s l25 and l19
L26           13 L25 AND L19

=> s l26 not py>2002
       3691294 PY>2002
L27            9 L26 NOT PY>2002

=> d ibib 1-9

L27  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2001:338762  CAPLUS
DOCUMENT NUMBER:          134:362292
TITLE:                    Methods of determining individual hypersensitivity to
                          a pharmaceutical agent from gene expression profile
INVENTOR(S):              Farr, Spencer
PATENT ASSIGNEE(S):       Phase-1 Molecular Toxicology, USA
SOURCE:                   PCT Int. Appl., 222 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

L27 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:120343 CAPLUS
DOCUMENT NUMBER: 54:120343
ORIGINAL REFERENCE NO.: 54:23042c-e
TITLE: Comparison of toxicity and **diuretic** action of **bismuth** compounds and mersalyl
AUTHOR(S): Heidenreich, O.; Reus, E.; Schneider, W.
CORPORATE SOURCE: Univ. Freiburg i. Br., Germany
SOURCE: Naunyn-Schmiedebergs Archiv fuer Experimentelle Pathologie und Pharmakologie (1960), 238, 270-80
CODEN: AEPPAE; ISSN: 0365-2009
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:120342 CAPLUS
DOCUMENT NUMBER: 54:120342
ORIGINAL REFERENCE NO.: 54:23042b-c
TITLE: Site of action of **diuretic bismuth** compounds
AUTHOR(S): Heidenreich, O.; Schneider, W.
CORPORATE SOURCE: Univ. Freiburg i. Br., Germany
SOURCE: Naunyn-Schmiedebergs Archiv fuer Experimentelle Pathologie und Pharmakologie (1960), 238, 258-69
CODEN: AEPPAE; ISSN: 0365-2009
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:120341 CAPLUS
DOCUMENT NUMBER: 54:120341
ORIGINAL REFERENCE NO.: 54:23042a-b
TITLE: Diuresis with water-soluble organic **bismuth** compounds in dogs
AUTHOR(S): Heidenreich, O.; Schneider, W.
CORPORATE SOURCE: Univ. Freiburg i. Br., Germany
SOURCE: Naunyn-Schmiedebergs Archiv fuer Experimentelle Pathologie und Pharmakologie (1960), 238, 245-57
CODEN: AEPPAE; ISSN: 0365-2009
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1937:8307 CAPLUS
DOCUMENT NUMBER: 31:8307

ORIGINAL REFERENCE NO.: 31:1095e-g
TITLE: Actions of **diuretic** drugs and changes in metabolites in edematous patients
AUTHOR(S): Stockton, A. B.
SOURCE: Archives of Internal Medicine (1936), 58, 891-900
CODEN: AIMDAP; ISSN: 0003-9926
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1931:11684 CAPLUS
DOCUMENT NUMBER: 25:11684
ORIGINAL REFERENCE NO.: 25:1289i,1290a
TITLE: **Diuretic** action of cacodylate of **bismuth**
AUTHOR(S): Besnier, A.
SOURCE: Journal de Pharmacie et de Chimie (1930), 11, 465-78
CODEN: JPHCA9; ISSN: 0368-3591
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1930:54021 CAPLUS
DOCUMENT NUMBER: 24:54021
ORIGINAL REFERENCE NO.: 24:5860i
TITLE: Comparative **diuretic** actions of **bismuth**, digitalis and theophylline; changes in blood and urinary metabolites in edema
AUTHOR(S): Stockton, A. B.
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1930), 27, 721-2
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1928:33359 CAPLUS
DOCUMENT NUMBER: 22:33359
ORIGINAL REFERENCE NO.: 22:3932b-c
TITLE: **Bismuth** as a **diuretic**
AUTHOR(S): Mehrtens, H. G.; Hanzlik, P. J.; Marshall, D. C.; Brown, N. S.
SOURCE: JAMA, the Journal of the American Medical Association (1928), 91, 223-5
CODEN: JAMAAP; ISSN: 0098-7484
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

L27 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1923:14213 CAPLUS
DOCUMENT NUMBER: 17:14213
ORIGINAL REFERENCE NO.: 17:2325g-h
TITLE: **Diuretic** action of **bismuth**; mechanism of this action
AUTHOR(S): Blum, Leon
SOURCE: Comptes Rendus des Seances de la Societe de Biologie et de Ses Filiales (1923), 88, 461-3
CODEN: CRSBAW; ISSN: 0037-9026
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

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     FILE 'MEDLINE' ENTERED AT 11:18:26 ON 29 MAR 2006
L1          5212 S BISMUTH
L2            93 S ACTINIUM
L3          1693 S DMPS OR DMSA
L4             1 S L3 AND L2
L5             7 S L3 AND L1
L6        638909 S KIDNEY OR RENAL OR NEPHRO?
L7             5 S L6 AND L5
L8            12 S L2 AND L6
L9        303767 S ACCUM? OR RETEN?
L10            4 S L9 AND L8
L11          646 S TOX
L12       543991 S TOX?
L13            1 S L12 AND L10
L14           12 S FRANCIUM
L15            1 S L14 AND L6

     FILE 'CAPLUS' ENTERED AT 11:25:59 ON 29 MAR 2006
L16       127908 S BISMUTH
L17         2530 S ACTINIUM
L18         1149 S DMPS OR DMSA
L19       337893 S KIDNEY OR RENAL OR NEPHRO?
L20           32 S L19 AND L17
L21            1 S L20 AND L18
L22            4 S L20 AND ADJUVANT
L23        25120 S DIURETIC OR LASIX OR FUROSEMIDE
L24            2 S L23 AND L20
L25           44 S L23 AND L16
L26           13 S L25 AND L19
L27            9 S L26 NOT PY>2002

=> s l23 and l20
L28            2 L23 AND L20

=> d ibib 1-2

L28  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:467296  CAPLUS
DOCUMENT NUMBER:          143:93157
TITLE:                    Efforts to Control the Errant Products of a Targeted
                          In vivo Generator
AUTHOR(S):                Jaggi, Jaspreet Singh; Kappel, Barry J.; McDevitt,
                          Michael R.; Sgouros, George; Flombaum, Carlos D.;
                          Cabassa, Catalina; Scheinberg, David A.
CORPORATE SOURCE:         Molecular Pharmacology and Chemistry Program,
                          Sloan-Kettering Cancer Center, New York, NY, 10021,
                          USA
SOURCE:                   Cancer Research (2005), 65(11), 4888-4895
                          CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:                American Association for Cancer Research
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          41    THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:802241  CAPLUS
DOCUMENT NUMBER:          141:273653
TITLE:                    Methods of protection from toxicity of alpha emitting
                          elements during radioimmunotherapy
```

INVENTOR(S): Scheinberg, David; McDevitt, Michael R.; Jaggi, Jaspreet
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004191169	A1	20040930	US 2004-806905		20040323
AU 2004273775	A1	20050331	AU 2004-273775		20040323
PRIORITY APPLN. INFO.:			US 2003-457503P	P	20030325
			WO 2004-US8817	W	20040323

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COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	44.51	52.05

FILE 'PCTFULL' ENTERED AT 11:30:48 ON 29 MAR 2006

FILE LAST UPDATED: 3 JAN 2006 <20060103/UP>
MOST RECENT UPDATE WEEK: 200552 <200552/EW>

FILE LAST UPDATED (FULLTEXT) 28 MAR 2006 <20060328/UPTX>
MOST RECENT UPDATE WEEK: 200612
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE. USE IPC7 FORMAT FOR SEARCHING THE IPC. WATCH THIS SPACE FOR FURTHER DEVELOPMENTS AND SEE OUR NEWS SECTION FOR FURTHER INFORMATION

>>> UPDATING OF BIBLIOGRAPHIC DATA DELAYED DUE TO DELIVERY FORMAT CHANGES <<<

>>> FULL-TEXT UPDATES CONTINUE. PATENT NUMBER AVAILABLE FOR DISPLAY ONLY, USE FIELD CODE FPI <<<

>>> SDI SEARCHES (ALERTS) WILL BE RESUMED WHEN BIBLIOGRAPHIC DATA BECOME AVAILABLE <<<

=> file dissab
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.16	53.21

FILE 'DISSABS' ENTERED AT 11:31:00 ON 29 MAR 2006

FILE COVERS 1861 TO 27 MAR 2006 (20060327/ED)

PARTICULAR PURPOSE, AND SHALL NOT BE LIABLE FOR DAMAGES OF ANY
KIND OR LOST PROFITS OR OTHER CLAIMS RELATED TO THE LICENSED
MATERIALS OR THEIR USE.

```
=> s bismuth
L29        1289 BISMUTH

=> s diuretic or DMSA or DMPS
            263 DIURETIC
            162 DIURETICS
            386 DIURETIC
                  (DIURETIC OR DIURETICS)
             37 DMSA
             32 DMPS
L30         452 DIURETIC OR DMSA OR DMPS

=> s l30 and l29
L31           0 L30 AND L29

=> s actinium
L32          18 ACTINIUM

=> s kidney or renal or nephro?
           5647 KIDNEY
            966 KIDNEYS
           6148 KIDNEY
                  (KIDNEY OR KIDNEYS)
           4211 RENAL
              4 RENALS
           4213 RENAL
                  (RENAL OR RENALS)
            982 NEPHRO?
L33        9161 KIDNEY OR RENAL OR NEPHRO?

=> s l33 and l32
L34           0 L33 AND L32

=> s l33 and l29
L35           5 L33 AND L29

=> d ibib 1-5

L35  ANSWER 1 OF 5  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   1999:58066  DISSABS   Order Number: AAIC719405 (not
                    available for sale by UMI)
TITLE:              DEVELOPMENT OF RADIOLABELED MONOCLONAL ANTIBODY CONSTRUCTS
                    CAPABLE OF TRANSPORTING HIGH RADIATION DOSE INTO CANCER
                    CELLS (BISMUTH, HUM195, IODINATION)
AUTHOR:             NIKULA, TUOMO [DR.PHIL.]
CORPORATE SOURCE:   JYVASKYLAN YLIOPISTO (FINLAND) (0979)
SOURCE:             Dissertation Abstracts International, (1998) Vol. 60, No.
                    3C, p. 616. Order No.: AAIC719405 (not available for sale
                    by UMI). UNIVERSITY OF JYVASKYLA, SEMINAARINK. 15,
                    FIN-40100 JYVASKYLA, FINLAND. 45 pages.
                    ISBN: 951-39-0120-3.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English

L35  ANSWER 2 OF 5  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   91:11615  DISSABS   Order Number: AAR9130604
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TITLE: CISPLATIN **NEPHROTOXICITY**, PROTECTIVE STRATEGIES, AND **KIDNEY** METAL INTERACTIONS AT NORMOTHERMIC AND HYPERTHERMIC TEMPERATURES (NORMOTHERMIC TEMPERATURES)
AUTHOR: DEWOSKIN, ROBERT SHELLEY [PH.D.]; RIVIERE, JIM E. [advisor]
CORPORATE SOURCE: NORTH CAROLINA STATE UNIVERSITY (0155)
SOURCE: Dissertation Abstracts International, (1991) Vol. 52, No. 5B, p. 2512. Order No.: AAR9130604. 164 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

L35 ANSWER 3 OF 5 DISSABS COPYRIGHT (C) 2006 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 87:13513 DISSABS Order Number: AAR8720924
TITLE: INVESTIGATIONS INTO THE MECHANISM OF ACTION OF THE TOXIC SESQUITERPENE LACTONES, HELENALIN AND HYMENOXON
AUTHOR: MERRILL, JILL CHRISTINE [PH.D.]
CORPORATE SOURCE: TEXAS A&M UNIVERSITY (0803)
SOURCE: Dissertation Abstracts International, (1987) Vol. 48, No. 6B, p. 1615. Order No.: AAR8720924. 156 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

L35 ANSWER 4 OF 5 DISSABS COPYRIGHT (C) 2006 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 87:10878 DISSABS Order Number: AAR8716575
TITLE: RADIOLABELED ANTIBODY IN TUMOR IMAGING AND THERAPY: IODINE AND RADIOMETAL CHELATES
AUTHOR: BERG, WENDIE TERESE ANDERSON [PH.D.]
CORPORATE SOURCE: THE JOHNS HOPKINS UNIVERSITY (0098)
SOURCE: Dissertation Abstracts International, (1987) Vol. 48, No. 5B, p. 1310. Order No.: AAR8716575. 265 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

L35 ANSWER 5 OF 5 DISSABS COPYRIGHT (C) 2006 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 80:11760 DISSABS Order Number: AAR8021652
TITLE: THE ULTRASTRUCTURAL DELINEATION OF THE LAMINA RARA EXTERNA MEMBRANE IN THE GLOMERULAR BASEMENT MEMBRANE OF NORMAL AND **NEPHROTIC** RATS, MICE AND HUMANS
AUTHOR: PILIA, PATRICIA ANN [PH.D.]
CORPORATE SOURCE: MEDICAL UNIVERSITY OF SOUTH CAROLINA (0122)
SOURCE: Dissertation Abstracts International, (1980) Vol. 41, No. 4B, p. 1320. Order No.: AAR8021652. 303 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

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L35 ANSWER 1 OF 5 DISSABS COPYRIGHT (C) 2006 ProQuest Information and

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TI DEVELOPMENT OF RADIOLABELED MONOCLONAL ANTIBODY CONSTRUCTS CAPABLE OF TRANSPORTING HIGH RADIATION DOSE INTO CANCER CELLS (**BISMUTH**, HUM195, IODINATION)
AB . . . of HuM195 to CHX-A-DTPA resulted in the attachment of up to 10 ligand molecules per antibody, and labeling efficiency with **Bismuth**-213 was typically over 90%. After injection into mice, there was no uptake or loss of **bismuth** to mouse tissues, that do not express antigen or to **kidney**, which has avidity for free, unbound **bismuth**. Toxicity of $\sp{213}$Bi-CHX-A-DTPA was evaluated in normal mice with doses from 0.5 to 20 mCi/kg showing no toxicity, but atomic . . $\sp{213}$Bi labeled conjugate showed dose and specific activity dependent killing of HL60 cells.

The results of this thesis indicate that **bismuth**-213 labeled HuM195 has high potency to specifically kill the target cells without remarkable toxicity to other tissues.

=> d his

(FILE 'HOME' ENTERED AT 11:18:17 ON 29 MAR 2006)

FILE 'MEDLINE' ENTERED AT 11:18:26 ON 29 MAR 2006

L1	5212	S	BISMUTH
L2	93	S	ACTINIUM
L3	1693	S	DMPS OR DMSA
L4	1	S	L3 AND L2
L5	7	S	L3 AND L1
L6	638909	S	KIDNEY OR RENAL OR NEPHRO?
L7	5	S	L6 AND L5
L8	12	S	L2 AND L6
L9	303767	S	ACCUM? OR RETEN?
L10	4	S	L9 AND L8
L11	646	S	TOX
L12	543991	S	TOX?
L13	1	S	L12 AND L10
L14	12	S	FRANCIUM
L15	1	S	L14 AND L6

FILE 'CAPLUS' ENTERED AT 11:25:59 ON 29 MAR 2006

L16	127908	S	BISMUTH
L17	2530	S	ACTINIUM
L18	1149	S	DMPS OR DMSA
L19	337893	S	KIDNEY OR RENAL OR NEPHRO?
L20	32	S	L19 AND L17
L21	1	S	L20 AND L18
L22	4	S	L20 AND ADJUVANT
L23	25120	S	DIURETIC OR LASIX OR FUROSEMIDE
L24	2	S	L23 AND L20
L25	44	S	L23 AND L16
L26	13	S	L25 AND L19
L27	9	S	L26 NOT PY>2002
L28	2	S	L23 AND L20

FILE 'PCTFULL' ENTERED AT 11:30:48 ON 29 MAR 2006

FILE 'DISSABS' ENTERED AT 11:31:00 ON 29 MAR 2006

L29	1289	S	BISMUTH
L30	452	S	DIURETIC OR DMSA OR DMPS
L31	0	S	L30 AND L29
L32	18	S	ACTINIUM
L33	9161	S	KIDNEY OR RENAL OR NEPHRO?
L34	0	S	L33 AND L32

```
L35             5 S L33 AND L29

=> s dimercapto?
L36            78 DIMERCAPTO?

=> s dithiol
              124 DITHIOL
               51 DITHIOLS
L37           163 DITHIOL
                  (DITHIOL OR DITHIOLS)

=> s l37 and l29
L38             1 L37 AND L29

=> d ibib

L38  ANSWER 1 OF 1  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
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ACCESSION NUMBER:   2004:23871  DISSABS   Order Number: AAI3100638
TITLE:              NMR and molecular modeling of the heavy-metal complexes of
                    phytochelatins and the cis/trans isomerization kinetics of
                    proline-containing peptides
AUTHOR:             Spain, Stephen Micheal [Ph.D.]; Rabenstein, Dallas L.
                    [advisor]
CORPORATE SOURCE:   University of California, Riverside (0032)
SOURCE:             Dissertation Abstracts International, (2003) Vol. 64, No.
                    8B, p. 3798. Order No.: AAI3100638. 402 pages.
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MOST RECENT UPDATE WEEK:       200552        <200552/EW>

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MOST RECENT UPDATE WEEK:         200612
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```
=> s bismuth
          9440 BISMUTH
             5 BISMUTHS
L39       9442 BISMUTH
                 (BISMUTH OR BISMUTHS)

=> s actinium
L40        280 ACTINIUM

=> s kidney or renal or nephro?
         40851 KIDNEY
          7981 KIDNEYS
         43727 KIDNEY
                 (KIDNEY OR KIDNEYS)
         26530 RENAL
            33 RENALS
         26538 RENAL
                 (RENAL OR RENALS)
          9964 NEPHRO?
L41      56957 KIDNEY OR RENAL OR NEPHRO?

=> s radioimmunother?
L42        679 RADIOIMMUNOTHER?

=> s l42 and l41
L43        499 L42 AND L41

=> s l43 and l40
L44         63 L43 AND L40

=> s diuretic and l44
          2758 DIURETIC
          3995 DIURETICS
          5819 DIURETIC
                 (DIURETIC OR DIURETICS)
L45          2 DIURETIC AND L44

=> d ibib 1-2

L45    ANSWER 1 OF 2     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2005120588 PCTFULL  ED 20051228  EW 200551
TITLE (ENGLISH):         PEPTIDES DELIVERED TO CELL NUCLEI
TITLE (FRENCH):          PEPTIDES DELIVRES A DES NOYAUX CELLULAIRES
INVENTOR(S):             QUINN, Thomas, P., 5700 Sinclair Road, Columbia, MO
                         65203, US [US, US];
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                         [IT, US]
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                         YUBIN, Miao, 5141 W. Louisville Ct., Columbia, MO
                         65203, US [CN, US], for US only;
                         GALLAZZI, Fabio, 4303 Jeana Ct., Columbia, MO 65203, US
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AGENT:                   HIGHLANDER, Steven, J.$, Fulbright & Jaworski L.L.P.,
                         600 Congress Avenue, Suite 2400, Austin, TX 78701$, US
LANGUAGE OF FILING:      English
LANGUAGE OF PUBL.:       English
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DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005120588	A2	20051222

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LT LU MC NL PL PT RO SE SI SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2005-US18700 A 20050526

PRIORITY INFO.: US 2004-60/574,558 20040526

L45 ANSWER 2 OF 2 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 2005028021 PCTFULL ED 20050405 EW 200513

TITLE (ENGLISH): METHODS FOR PROTECTION FROM TOXICITY OF ALPHA EMITTING ELEMENTS DURING **RADIOIMMUNOTHERAPY**

TITLE (FRENCH): PROCEDE DE PROTECTION CONTRE LA TOXICITE D'ELEMENTS D'EMISSION DE PARTICULES ALPHA LORS DE LA **RADIOIMMUNOTHERAPIE**

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McDEVITT, Michael, R., 5644 Netherland Avenue, Bronx, NY 10471, US;
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LANGUAGE OF FILING: English

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DOCUMENT TYPE: Patent

PATENT INFORMATION:

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WO 2005028021	A2	20050331

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RW (ARIPO): BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO SE SI SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2004-US8817 A 20040323

PRIORITY INFO.: US 2003-60/457,503 20030325

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L15            1 S L14 AND L6

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L22            4 S L20 AND ADJUVANT
L23        25120 S DIURETIC OR LASIX OR FUROSEMIDE
L24            2 S L23 AND L20
L25           44 S L23 AND L16
L26           13 S L25 AND L19
L27            9 S L26 NOT PY>2002
L28            2 S L23 AND L20

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     FILE 'DISSABS' ENTERED AT 11:31:00 ON 29 MAR 2006
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L31            0 S L30 AND L29
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L33         9161 S KIDNEY OR RENAL OR NEPHRO?
L34            0 S L33 AND L32
L35            5 S L33 AND L29
L36           78 S DIMERCAPTO?
L37          163 S DITHIOL
L38            1 S L37 AND L29

     FILE 'PCTFULL' ENTERED AT 11:34:13 ON 29 MAR 2006
L39         9442 S BISMUTH
L40          280 S ACTINIUM
L41        56957 S KIDNEY OR RENAL OR NEPHRO?
L42          679 S RADIOIMMUNOTHER?
L43          499 S L42 AND L41
L44           63 S L43 AND L40
L45            2 S DIURETIC AND L44

=> s DMPS and l44
          140 DMPS
L46           1 DMPS AND L44

=> d kwic
```

L46 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN
TIEN METHODS FOR PROTECTION FROM TOXICITY OF ALPHA EMITTING ELEMENTS DURING **RADIOIMMUNOTHERAPY**
TIFR PROCEDE DE PROTECTION CONTRE LA TOXICITE D'ELEMENTS D'EMISSION DE PARTICULES ALPHA LORS DE LA **RADIOIMMUNOTHERAPIE**
ABEN Provided herein are methods of reducing **nephrotoxicity** form at least one alpha particle-emitting daughter of **actinium**-225 during **radioimmunotherapeutic** treatment for a pathophysiological condition, methods of improving **radioimmunotherapeutic** treatment of cancer and methods of increasing the therapeutic index of an **actinium**-225 radioimmunoconjugate during treatment of a pathophysiological condition. Adjuvants effective for preventing accumulation of<sp>225</sp>Ac daughters within the **kidneys** are administered during treatment with an **actinium**-225 radioimmunoconjugate to reduce **nephrotoxicity**. Examples of adjuvants are chelators, diuretics and/or competitive metal blockers.
ABFR La presente invention a trait a des procedes de reduction de la **nephrotoxicite** derivee d'au moins un produit de filiation d'emission de particules alpha d'**actinium** 225 lors d'un traitement de **radioimmunotherapie** pour une condition pathophysiologique, des procedes d'amelioration de traitement de **radioimmunotherapie** du cancer et des procedes d'accroissement de l'indice therapeutique d'un conjugue radioimmunologique d'**actinium** 225 lors d'un traitement d'une condition pathophysiologique. Des adjuvants efficaces pour la prevention d'accumulation de produits de filiation d'**actinium** 225 dans les reins sont administres lors du traitement avec un conjugue radioimmunologique d'**actinium** 225 pour reduire la **nephrotoxicite**. Des exemples d'adjuvants sont des chelateurs, des diuretiques et/ou des agents de blocage de metaux par competition.

DETD Field of the Invention
The present invention relates generally to the fields of **radioimmunotherapy** and cancer treatment. Specifically, the present invention provides methods of protecting an individual from toxicity of alpha particle-emitting elements during radioinimunotherapy.

Radioimmunotherapyhas advanced tremendouslyin the last 20 years with the development of more sophisticated carriers, as well as of radionuclides optimized for 3 a particular cancer and therapeutic application (52). **Radioimmunotherapy** (RIT) with alpha particle emitting radionuclides is advantageous because alpha particles have high LET and short path lengths (50-80[tm) (53-57). Therefore, a. . . . or be transported to various target organs where they can accumulate and cause radiotoxicity. Bismuth is known to accumulate in the **renal** cortex (66-69). It has been observed that after injection in mice, francium rapidly accumulates in the **kidneys** (unpublished result). Francium distribution in the body has not been described due to its 5 short half-life that makes experimental study difficult. . .

Monkeys injected with escalating doses of the untargeted 225 Ac nanogeneratordevelopeda delayed radiationnephropathy manifestingas

anemia and **renal**
failure (63). Therefore, a possible hindrance to the development of these agents as safe
and effective cancer therapeutics is likely to be their **nephrotoxicity**. By preventing the
0 **renal** accumulation of the radioactive daughters or by accelerating their clearance from the
body, the therapeutic-index of the 225Ac nanogenerator could be. . .
.
Tr have
relativelylongerhalf-livesof 45.6min. and4.9
min.,respectively,andtherefore,have the
potential to cause radiation damage (61,59). The presence of bismuth-binding,
metallothionein-like proteins in the cytoplasm of **renal**
proximal tubular cells, makes the
kidney a prime target for the accumulation of free,
radioactive bismuth (66-68). Dithiol
chelators have been shown to chelate bismuth and enhance. . .
.
increase
urine output and accelerate the elimination of sodium and potassium in urine, by
inhibiting their reabsorption in different segments of the **nephron** (75).
.
prior art is lacking in methods of using, individually or in combination,
adjuvant chelation, diuresis or competitive metal blockade to reduce **nephrotoxicity** from
225 Ac daughters generated during **radioimmunotherapy**. The present invention fulfills this
5 long-standing need and desire in the art.
.
treatment of a pathophysiological
condition. A phan-nacologically effective dose of at least one adjuvant effective for
preventing accumulation of a metal in **kidneys** and an **actinium**-225
radioimmunoconjugateto treat the pathophysiologicalconditionare administeredto the
individual. Accumulation of an alpha particle-emitting daughter of the **actinium**-225
5 within the **kidneys** of the individual is prevented via interaction between the adjuvant
and the 225 Ac daughter or the **kidney** tissue or a combination thereof thereby reducing
nephrotoxicity during the **radioimmunotherapeutic**
treatment.

The present invention is directed to related methods of reducing
nephrotoxicity in an individual by administering a diuretic alone or in combination with
6
the chelator and administering an **actinium**-225
radioimmunoconjugate to treat the
pathophysiological condition. The chelator scavenges bismuth-213 daughters of
actinium The diuretic inhibits reabsorpfion of francium-21 I daughters of **actinium**-
225 within the **kidneys** to prevent accumulation thereof to reduce **nephrotoxicity**.

The present invention also is directed to a method of improving **radioimmunotherapeutic** treatment of cancer in an individual. As described above a pharmacologically effective dose of a chelator and an **actinium**-225 radioimmunoconjugateare administeredindividually. The chelator scavenges bismuth-213 daughters of the **actinium**-225 to reduce **nephrotoxicity** in the individual during treatment thereby increasing the therapeutic index of the **actinium**-225 to improve the treatment for cancer.

The present invention also is directed to related methods of improving **radioimmunotherapeutic** treatment of cancer by reducing **nephrotoxicity** in the individual during treatment thereby increasing the therapeutic index of the **actinium**-225 to improve 5 the treatment for the cancer. A diuretic alone or in combination with the chelator and an **actinium**-225radioimmunoconjugateareadministeredindividuallytot heindividual. The chelator functions as described above. The diuretic inhibits **renal** uptake of francium-21 I daughters within the **kidneys** to reduce **nephrotoxicity**.

The present invention is directed further to a method of increasing the 0 therapeutic index of an **actinium**-225 radioimmunoconjugate during treatment of a pathophysiological condition in an individual. **Renal** uptake of at least one alpha particle-emitting daughter of **actinium**-225 is inhibited whereby **nephrotoxicity** is reduced during the treatment thereby increasing the therapeutic index of said **actinium**-225 radioimmunoconjugate. In related methods inhibition of **renal** uptake of 225 Ac 5 daughters is accomplished by administering a phan-nacologically effective amount of an adjuvant comprising a chelator to scavenge the 225 Ac daughters therewith or of a diuretic to inhibit reabsorption of the 225 Ac daughters within a **kidney** or of a competitive metal blocker to prevent binding of 21 'Bi within a **kidney** or a combination of a chelator, a diuretic and the competitive metal blocker.

1 5 Figure 2 depicts the structures of 2,3 dimercapto-·I -propanesulfonic acid (**DMPS**) and meso 2,3 dimercaptosuccinic acid (DMSA)
Figures 3A-3B compare the effect of dithiol chelators on 213 Bi distribution in **kidneys** and blood. Figure 3A compares reduction in the **renal** 213 Bi activity by **DMPS** or DMSA treatment at 6 hours and 72 hours post-injection. The **renal** 2 0 22 1 Fr activity is unchanged at both time-points. Figure 3B compares the increase in the 213 Bi activity in blood by chelation therapy with **DMPS** or DMSA at 6 hours and 72 hours post injection. Data are mean (SE). %ID/g = percentage of injected dose per. . .

Figures 4A-4B depict the effect of diuresis or a combination of metal chelation and diuresis on **renal** 22'Fr and 21 'Bi activity. Figure 4A shows the reduction in the 24 hour **renal** 22 'Fr and2Bi activities by furosemide and chlorothiazide (CTZ) treatment. Figure 4B shows the reduced **renal** accumulation of 22 'Fr and 21 'Bi at 24 hours post-injectionby combinationtherapy with **DMPS** andfurosemideor CTZ. Data are mean (SE). %lD/g = percentage of injected dose per gram of tissue.

8

Figure 5 depicts the effect of competitive metal blockade on 22'Ac daughter distribution and shows the reduction in the **renal** 213 Bi activity by bismuth subnitrate (BSN) at 6 hours and 24 hours post-injection.

animal to that of a non tumor-bearing mouse of the same strain. Figure 6B shows the reduction in the ratio of **kidney** to femur activity for 22'Ac and 2 Bi in animals with higher tumor burden. **DMPS** treatment further reduced the **kidney** to femur activity ratio for 213 Bi. Figure 6C shows the reduction in the **renal** 213 Bi activity by the presence of higher tumor burden, and further enhancement of the effect by concomitant **DMPS** treatment. Error bars denote SE.

Figure 7 depicts the biodistribution of [Ac]Huml95 at 24 hours in **DMPS**-treated and untreated monkeys.

DETAILED DESCRIPTION OF THE INVENTION

In one embodiment of the present invention there is provided a method of reducing **nephrotoxicity** in an individual during **radioimmunotherapeutic** treatment of 2 0 a pathophysiological condition comprising administering a pharmacologically effective dose of at least one adjuvant effective for preventing accumulation of a metal in **kidneys;** administering an **actinium**-225 radioimmunoconjugate to treat the pathophysiological condition; and preventing accumulation of alpha particle-emitting daughters of the **actinium**-225 within the **kidneys** of the individual via interaction between the adjuvant 2 5 and the 225 Ac daughters or the **kidney** tissue or a combination thereof thereby reducing **nephrotoxicity** during the **radioimmunotherapeutic** treatment. In an aspect of this embodiment the adjuvant(s) may be administeredprior to administering the **actinium**-225 radioimmunoconjugate with the adjuvant(s) continuing to be administered after the **actinium**-225 radioimmunoconjugate.

or bismuth subcitrate. In these aspects the 225 Ac daughter may be bismuth-213, francium-221 or a combination thereof In all aspects the **actinium**-225 radioimmunoconjugate may comprise an 0 **actinium**-225 bifimctional chelant and a monoclonal antibody. An example of such a radiolmmunoconjugate is [225 Ac] DOTA-HuM195. Further to all aspects the

pathophysiological. . .

In a related embodiment there is provided a method of reducing **nephrotoxicity** in an individual during **radioimmunotherapeutic** treatment of a pathophysiological condition comprising administering a pharmacologically effective dose of a chelator; administering an **actinium**-225 radioimmunoconjugate to treat the cancer; and preventing accumulation of bismuth-213 daughters of the **actinium**-225 within the **kidneys** of the individual by scavenging thereof with the chelator thereby reducing **nephrotoxicity** during the **radioimmunotherapeutic** treatment.

Further to this embodiment the method comprises administering a pharmacologicallyeffectivedose of a diureticand preventingaccurnulationof francium-211 daughters of the **actinium**-225 within the **kidneys** of the individual by inhibiting reabsorption of francium-211 thereinwith the diuretic thereby reducingnephrotoxicity during the radiolmmunotherapeutic treatment.

In another related embodiment there is provided a method of reducing **nephrotoxicity** in an individual during **radioimmunotherapeutic** treatment of a pathophysiological. condition comprising administering a pharmacologically effective dose of a diuretic; administering an **actinium**-225 radioiminunoconjugate to treat the cancer; and preventing accumulation of francium-21 1 daughters of the **actinium**-225 within the **kidneys** of the individualby inhibiting reabsorption of francium-21 I therein with the diuretic thereby reducing **nephrotoxicity** during the **radioimmunotherapeutic** treatment.

In another embodiment of the present invention there is provided a method of improving **radioimmunotherapeutic** treatment of a cancer in an individual, comprising administering a pharmacologically effective dose of a chelator; administering an **actinium**-225 radioimmunoconjugate; and scavenging bismuth-213 daughters of the **actinium**-225 with the chelator to reduce **nephrotoxicity** in the individual during the treatmentthereby increasingthe therapeutic index of the **actinium**-225 to improve the treatment for cancer. Further to this embodiment there is provided a method of administering a pharmacologically effective dose of a diuretic; and inhibiting **renal** uptake of francium-21 1 daughters of the **actinium**-225 with the diuretic to reduce **nephrotoxicity** in the individual during the treatment thereby increasing the therapeutic index of the **actinium**-225 to improve the treatment for the cancer.

In a related embodiment there is provided a method of improving **radioimmunotherapeutic** treatment of cancer in an individual, comprising administering a pharmacologically effective dose of a diuretic; administering an **actinium**-225 radioimmunoconjugate; and inhibiting **renal** uptake of francium-211 daughters of the **actinium**-225 with the diuretic to reduce **nephrotoxicity** in the individual during the treatment thereby increasing the therapeutic index of the **actinium**-225 to improve the treatment for the cancer.

In yet another embodiment there is provided a method of increasing the therapeutic index of an **actinium**-225 radioimmunoconjugate during treatment of a pathophysiological condition in an individual comprising inhibiting **renal** uptake of at least one alpha particle-emitting daughter of **actinium**-225 whereby **nephrotoxicity** is reduced during the treatment thereby increasing the therapeutic index of the **actinium**-225 radioimmunoconjugate.

In an aspect of this embodiment the step of inhibiting **renal** uptake comprises administering a pharmacologically effective amount of an adjuvant comprising a chelator to scavenge the 225 Ac daughters therewith or of a diuretic to inhibit reabsorption of the 225 Ac daughters within a **kidney**, or a competitive metal blocker to prevent binding of said 225 Ac daughters within a **kidney** or a combination thereof An example of an 225 Ac daughtz]r scavengedby a chelator is bismuth An example of an 225 Ac daughter that is inhibited from reabsorbing into the **kidneys** is francium-21 1. An example of an 225 Ac daughter that is prevented from binding within a **kidney** is 213 Bi.

5 As used herein **radioimmunotherapy** shall refer to targeted cancer therapy in which a radionuclide is directed to cancer cells by use of a specific antibody carrier.

,225Ac nanogenerator shall refer to a nano-scale, in-vivo generator of alpha particle emitting radionuclide daughters, produced by the attachment of a chelated **Actinium**-225 atom to a monoclonal antibody.

Provided herein are methods of controlling **renal** uptake of **actinium**-225 daughters generated by an 225 Ac nanogenerator during targeted **radioimmunotherapy** which accelerate the clearance of the alpha particle-emitting daughters from the body.

Methods utilizing metal chelation, diuresis, or competitive metal blockade may be used as adjunct therapies to modify the potential **nephrotoxicity** of

225 Ac daughters.

Generally, a radioimmunoconjugate comprising an 225 Ac nanogenerator will bind a
targeted tumor cell. Upon binding the **actinium**-255 decays and delivers the alpha
particle-emitting daughters to the cell to effect treatment. Once the decay cascade
sequence begins, however, thedaughter radiometals. . . are not delivered to the targeted tumor cell. Thus, the daughters are free to accumulate in healthy tissues such as the **kidneys** causing toxicity.

Chelated metals are protected and are, therefore, safe if detached from the
antibody due to their rapid **renal** clearance. Chelators such as, but not limited to, the
2 0 dithiol chelators 2,3 dimercapto-1-propane sulfonic acid (**DMPS**) and meso 2,3-
dimercapto succinic acid (DMSA) shown in Figure 2 or other chelators, e.g.,
ethylenediamine tetra-acetic acid (EDTA), diethylenetriamine pentaacetic acid. . . zinc diethylenetriamine
pentaacetic acid (Zn-DTPA),may be used to prevent the accumulation of free bismuth-
2 5 213 daughters in the patient. Preferably, **DMPS** is used to chelate bismuth-213
daughters.

The present invention also provides methods of using diuretics to reduce **renal** uptake of francium-211 daughters and, by extension as a decay product thereof,
bismuth-213 daughters into the **nephron** via inhibition of reabsorption of francium-21 I
1 3
through diuresis. Examples of such diuretics are furosemide, chlorthiazide,
hydrochlorothiazide, bumex, or other loop diuretic. Additionally, competitive metal
blockers may be used to compete with bismuth-213 for binding sites in the **renal** tubular
cells of the **kidney**. Examples of a nonradioactive bismuth competitor are bismuth
subnitrate or bismuth subcitrate.

chelators, diuretics or
competitive metal blockers, either individually or in combination, may be used as an
adjunct chelating therapy to modify the **nephrotoxicity** of bismuth-213 and/or francium-
21 1. Combination of adjuvant therapies results in cumulative effects over individual
1 0 therapies. Therefore, **nephrotoxicity** is reduced during treatment and larger and more
effective doses of the 225 Ac nanogenerator may be administered. This may allow. . .

1 5 In the 215Ac nanogenerator the **actinium**-225 may be stably bound to a
monoclonal antibody via a bifunctional chelant, such as a modified 1,4,7,10-
tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) which chelates the **actinium**-

225 while binding it to the monoclonal antibody. Although not limited to such, an
example of a radioimmunoconjugate (RIC) suitable for targeted. . .

Additionally,themethodsprovidedhereinaremoreefficaciousinreducing **nephrotoxicity** in patients with a higher tumor burden. The presence of high levels of a
specific target tumor burden caused a decrease. . .

1 4
It is contemplatedthat the adjunct methods describedherein maybe used with targeted 225Ac nanogeneratorradioiniinunotheiapy of pathophysiological conditions
benefiting from 225 Ac **radioimmunotherapy**. For example, the methods presented herein
may be used in conjunction with **radioimmunotherapeuticmethods** for treatment of solid
cancers, disseminated cancers and micrometastatic cancers. Thus, leukemias, such as
myeloidleukemia,maybenefitfromthisadjunettherapy. Itisfurthercontemplatedthat
other diseases or disorders for which 225. . .

0 The adjuvants of the present invention may be administered prior to the
225 Ac nanogenerator with continued administration after the **radioimmunotherapeutic**
treatment. Routes of administration may be either oral or via injection, such as
intravenous injection, and are well known to those of. . .

2 0 The adjuvants are administered in an amount to demonstrate a pharmacological effect, e.g., an amount to reduce **nephrotoxicity** due to bismuth-213 or
francium-21 I accumulation within the **kidneys**. An appropriate dosage may be a single
administered dose or multiple administered doses. The doses administered optimize
effectiveness against negative effects of **radioimmunotherapeutic** treatment. As with all
5 pharmaceuticals, including the 225 Ac nanogenerator described herein, the amount of the
adjuvant administered is dependent on. . . the patient, the patient's history,
the nature of the cancer treated, i.e., solid or disseminated, the amount and specific
activity of the **actinium** generator construct administered and the duration of the
radioimmunotherapeutic treatment.

typically fall within recommended usage
guidelines designated by the package inserts or by the general practice of medicine. For
example, doses of **DMPS** may be in the recommended range of 0. I-Immol/kg/d for the
treatment of heavy metal poisoning (64). An example of a dosing regimen for DMSA
may be about 10 mg/kg every 8 houts, and for **DMPS** may be 200-1500mg/day in divided
doses.

It is contemplated that use of the adjuvant therapies described herein atoms is substantially high provides for a significant reduction in

nephrotoxicity.

Therefore, with a capability to clear free **actinium**-225 daughters greater than the daughters generated for a given dose, higher doses of the 225 Ac nanogenerator may be administeredwithareducedriskofsubsequentnephrotoxicityduringtreatment. A-dose of about 0.5 [tCi/kg to about 5.0]tCi/kg of **actinium**-225 may be used to treat the patient.

A representative example is about 1]iCi/kg of **actinium** However, determination of dosage of the adjuvants described herein and of the 225Ac nanogenerator is well within the skill of an artisan. . .

EXAMPLE2
Preparation and qualfty control of **actinium**-225 labeled antibodies
22'Ac was conjugated to SJ25CI, a mouse anti-human CD19 IgG1 monoclonal antibody (Monoclonal Antibody Core Facility, Memorial Sloan Kettering Cancer Center). . .

EXANIPLE 3
1 5 Administration of **actinium**-225 nanogenerator to mice
The mice were anesthetized and then injected intravenously in the retro-orbital venous plexus with 0. 5 ptCi of. . .

EXAAWLE5
Free metal scavenging with **DMPS** or DMSA
Animals received either 2,3 -dimercapto- I -propanesulfonic acid (DMP S; I 0 Sigma, St. Louis, MO) or meso-2,3-dimereaptosuccinic acid (DMSA;. . .

Samples of blood taken by cardiac puncture, of **kidneys**, of liver and of small intestine were removed. The organs were washed in distilled water, blotted dry on of 21 2 gauze, weighed,. . .

The **renal** 213 Bi activity differed significantly between the **DMPS** or DMSA treated groups and untreated controls at 6 hours (ANOVA, $p < 0.0001$) and 72 hours (ANOVA, $p < 0.0001$) post-injection. . .

18
The 6 hour **renal** 213 Bi activity in the control group was 95.7 + 3.8 %ID/g, which was reduced to 38.6 5.5 %ID/g and 66.0 + 1.9 %ID/g in **DMPS** and DMSA treated groups, respectively. A similar reduction in the **renal** 213 Bi activity was observed at 72 hours post-injection of 66.7 + 7.9 %lD/g in controls versus 21.7 I 2.1 %ID/g and 41.4 7.3 in **DMPS** and DMSA treated groups, respectively. **DMPS** was significantlymore effective than DMSA in preventing the **renal** 213 Bi accumulation at both time-points (6h, $p < 0.001$; 72h, $p < 0.001$). The **renal** 22 1 Fr activity, however,

was not significantly different
between the experimental groups at either 6 hours (ANOVA, p = 0.39).

in Figure 3B, the mean blood 213 Bi activity was higher (6h,
ANOVA p< 0.0001; 72h, ANOVA p< 0.0001) in the **DMPS** (9.2 + 0.5
%ID/g and 5.
0. I %ID/g at 6 and 72 hours, respectively) and DMSA (5.8 I 0.5.
at 6 and 72 hours, respectively. However, the
blood 22'Fractivitywasunalteredbyehelationtherapy(datanotshown).
Similarresults
were seen with calcium-diethylenetriamine pentaacetate (Ca-DTPA), but it
was less
effective than **DMPS** in reducing the **renal** 213 Bi
activity (data not shown).

chelators are transported free or as disulfides with
plasma proteins and non-protein sulfhydryl compounds, e.g. cysteine
(79). In human
2 0 plasma, **DMPS** has been shown to form non-protein
sulfhydryls to a greater extent at
37%, than DMSA at 8%. Therefore,**DMPS** is thoughtto be more
reactive in plasma than
DMSA (79). Also, it is believedthat the presence of charged
carboxylgroups impede the
transport.

These factors may account for the greater effectiveness of **DMPS**
in
2 5 reducing the **renal** 213Bi uptake, as compared to DMSA.
DMPS, being more reactive, is
rapidly oxidized in aqueous solutions to form di-sulfides (81). However,
a loss of
efficacy was not observed when **DMPS** was administered in
drinking water. This
possibly is due to disulfide reduction in the **renal** tubular
cells by a glutathione-disulfide
exchange reaction, to yield the parent drug. This effect has been shown
in previous
1 9
studies (79).

to cause any significant toxicity due to
the short path length of alpha particles (50). In contrast, the
reduction in the **renal** 213 Bi
activity is critical to the safety of the 225Ac nanogenerators.

Alternatively, mice received **DMPS** (1.2 mg/ml in drinking
water) and
either furosemide or CTZ i.p using the same dose schedule as above. The
controls
2 0. hours post-injectionwith the labeled antibody and the mean
activity (%ID/g) of 22'Ac] 22 Tr and 213 Bi in blood and
kidneys was calculated for each
experimental group, as described above.

Diuretic therapy prevented the **renal** accumulation of both 22
'Fr and 2Bi
2 5 (Figure 4A). The 24 hour **renal** 22 Tr activity differed
significantly (ANOVA, p<0.000 1)
between the experimental groups (21.9 1.0 %ID/g in controls versus 1
1. 8 0.4 %ID/g
and 9.7 0.4 %ID/g in furosemide and CTZ treated groups, respectively).

Similarly, the
24 hour **renal** 213 Bi activity was 3 8.7 1.0 %ID/g in the
controls versus 18.3 + 0.6 %ID/g
and 18.6 1.6 %ID/g in. . .

Furthermore, the combination of **DMPS** with a diuretic,
furosemide or
CTZ, caused a greater reduction of 80% in the **renal** 213Bi
activity than seen with
DMPS or diuretics alone (Figures 4A-4B). The 24 hour
renal 213 Bi activity was 45.7
1.0 %ID/g in controls versus 10.4 1.0 %ID/g and 10.5 1.5 %ID/g in
DMPS +
furosemide and **DMPS** + CTZ groups, respectively (ANOVA,
p<0.0001). The
reduction in the **renal** 22 Tr accumulation, however, was
similar to that seen with diuretic
1 0 treatment (25.7 + 1.3 %ID/g in controls versus 9.7 0.4 %ID/g and
13.3 + 1.4 %ID/g in
DMPS + furosemide and **DMPS** + CTZ groups,
respectively (ANOVA, p<0.0001).
. . .
of the alkali
metals, Na+ or K+ or both, although they differ in their potency,
mechanism and site of
action within the **nephron**. Furosemide and CTZ act,
respectively, in the ascending limb
1 5 of Henle's loop and distal convoluted tubule of the **nephron**
(82). The significant drop
in the **renal** 22 Tr activity with furosemide and CTZ possibly
is due to an inhibitionof the
renal tubular reabsorption of 22 1 Fr which is an alkali metal
and is, therefore, expected to
behave like Na' and K]. Since 213 Bi is generated from 22 'Fr, a
decrease in the **renal** 213 Bi
ensued. Furthermore, the combinationof **DMPS** with a diuretic,
e.g., furosemide or CTZ,
2 0 resulted in an even greater reduction in **renal** 213 Bi
activity than seen with **DMPS** or the
diuretics alone. The administered doses of furosemide and CTZ were
scaled from
previously published literature on their ED50 in mice.. . .
. . .
24 hours after 225 Ac nanogenerator injection. The mean %ID/g of 22'Ac]
22 Tr
and 213 Bi in blood and **kidneys** at sacrifice-time was
calculated for each experimental
group.

Competitive blockade of 213 Bi binding-sites in the **renal**
tubular cells by
non-radioactivebismuth resultedin anioderate, but
significant,reductionin the **renal** 2 13 Bi
activity at both 6 hour ($p = 0.004$) and 24 hour ($p < 0.0001$) time-points
(Figure 5).

Renal 21313i activity at 6 and 24 hours post-injectionwas 57.5
2.4 %ID/g and 64.9 1.2
%ID/g, respectively in controls versus 46.1 1.4 %ID/g and 48.2 0.6
%ID/g,
respectively in B SN treated animals. As expected, the **renal*****
<------User Break------>

22 Tr activity was unaltered
(Figure 5) at either time-point (6 hours, p=0. 1 0; 24 hours, p=0.6 1).

5 EXAMPLE 8
Effect of **DMPS** on tumor burden
Disseminated human Daudi lymphorna (84) treated with 22'Ac labeled anti-CD19, was used as the model system. SCID mice, 10-12. . . or 7 days growth of tumor, high tumor burden or
0 30 days growth of tumor or high tumor burden + **DMPS** group or
30 days growth of
tumor and treated with 1.2mg/ml **DMPS** in drinking water, starting one day before
injection with 225 Ac nanogenerator. All mice were injected intravenously with 5xlO'
Daudi lymphorna cells. . .

. . .
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